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□1: Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 1999 Dec;21(6):493-6.

Related Articles, Links

**[Mode of action of sildenafil]**

**[Article in Chinese]**

**Wang J, Re J, Wang Z.**

Department of Urology, Xuan Wu Hospital, Beijing 100054.

Sildenafil is the first oral therapeutic agent for erectile dysfunction. Sildenafil is a selective inhibitor of cGMP-specific phosphodiesterase (PDE-5). Penile erection involves relaxation of the corpus cavernosum, an event mediated by NO and cGMP. The biological actions of cGMP are terminated by phosphodiesterase enzymes and PDE-5 is the major cGMP metabolising enzyme in this tissue. Sildenafil is relatively safe compared to erection injectables because it does not relax on isolated human corpus cavernosum, and does not cause priapism. Due to the tendency of abuse of sildenafil, its adverse cardiovascular associations with myocardial infarction, ventricular arrhythmia and hypertension need to be alerted.

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1: Trends Pharmacol Sci. 2000 Dec;21(12):484-9.

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**ELSEVIER**  
FULL-TEXT ARTICLE

### Pharmacotherapy for erectile dysfunction.

**Bivalacqua TJ, Champion HC, Hellstrom WJ, Kadowitz PJ.**

Department of Urology and Pharmacology, Tulane University School of Medicine, New Orleans, LA 70112, USA. tbivala@tulane.edu

Erectile dysfunction (ED) is defined as the consistent inability to obtain or maintain an erection for satisfactory sexual relations. An estimated 20-30 million men suffer from some degree of sexual dysfunction. The past 20 years of research on erectile physiology have increased our understanding of the biochemical factors and intracellular mechanisms responsible for corpus cavernosal smooth muscle contraction and relaxation, and revealed that ED is predominantly a disease of vascular origin. Since the advent of sildenafil (Viagra), there has been a resurgence of interest in ED, and an increase in patients presenting with this disease. A thorough knowledge of the physiology of erection is essential for future pharmacological innovations in the field of male ED.

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Related Articles, Links

**Sildenafil is a pulmonary vasodilator in awake lambs with acute pulmonary hypertension.****Weimann J, Ullrich R, Hromi J, Fujino Y, Clark MW, Bloch KD, Zapal WM.**Departments of Anesthesia and Critical Care, Respiratory Care, and Medicine,  
Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114,  
USA.

**BACKGROUND:** Phosphodiesterase type 5 (PDE5) hydrolyzes cyclic guanosine monophosphate in the lung, thereby modulating nitric oxide (NO)/cyclic guanosine monophosphate-mediated pulmonary vasodilation. Inhibitors of PDE5 have been proposed for the treatment of pulmonary hypertension. In this study, we examined the pulmonary and systemic vasodilator properties of sildenafil, a novel selective PDE5 inhibitor, which has been approved for the treatment of erectile dysfunction. **METHODS:** In an awake lamb model of acute pulmonary hypertension induced by an intravenous infusion of the thromboxane analog U46619, we measured the effects of 12.5, 25, and 50 mg sildenafil administered via a nasogastric tube on pulmonary and systemic hemodynamics ( $n = 5$ ). We also compared the effects of sildenafil ( $n = 7$ ) and zaprinast ( $n = 5$ ), a second PDE5 inhibitor, on the pulmonary vasodilator effects of 2.5, 10, and 40 parts per million inhaled NO. Finally, we examined the effect of infusing intravenous l-NAME (an inhibitor of endogenous NO production) on pulmonary vasodilation induced by 50 mg sildenafil ( $n = 6$ ). **RESULTS:** Cumulative doses of sildenafil (12.5, 25, and 50 mg) decreased the pulmonary artery pressure 21%, 28%, and 42%, respectively, and the pulmonary vascular resistance 19%, 23%, and 45%, respectively. Systemic arterial pressure decreased 12% only after the maximum cumulative sildenafil dose. Neither sildenafil nor zaprinast augmented the ability of inhaled NO to dilate the pulmonary vasculature. Zaprinast, but not sildenafil, markedly prolonged the duration of pulmonary vasodilation after NO inhalation was discontinued. Infusion of l-NAME abolished sildenafil-induced pulmonary vasodilation. **CONCLUSIONS:** Sildenafil is a selective pulmonary vasodilator in an ovine model of acute pulmonary hypertension. Sildenafil induces pulmonary vasodilation via a NO-dependent mechanism. In contrast to zaprinast, sildenafil did not prolong the pulmonary vasodilator action of inhaled NO.

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## Encyclopedia

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### Phosphodiesterase-5 inhibitors (PDE-5 inhibitors) for erection problems [Medication]

#### Topic Contents

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- [How It Works](#)
- [Why It Is Used](#)
- [How Well It Works](#)
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#### Examples

Brand Name	Chemical Name
Viagra	sildenafil citrate
Levitra	vardenafil
Cialis	tadalafil

Phosphodiesterase-5 inhibitors (PDE-5 inhibitors) are taken at least an hour before you plan to be sexually active. PDE-5 inhibitors will result in an erection only if you are sexually stimulated.

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#### How It Works

During an erection, blood fills tissue in the penis, causing it to enlarge and become stiff. The PDE-5 inhibitors relax smooth muscle, allowing the penis to fill with blood.

Stimulation of the penis is necessary for Levitra and Cialis to work; Viagra can produce a spontaneous erection in those men for whom it is effective.

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## Why It Is Used

PDE-5 inhibitors can be used when an erection problem (erectile dysfunction) is caused by:

Diabetes.

High blood pressure.

Spinal cord injury or other problems affecting nerve function.

Prostate surgery.

Side effects of medications.

Emotional or psychological causes.

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## How Well It Works

PDE-5 inhibitors are effective treatment for erection problems. A review of trials has shown that 83% of men with erection problems who used Viagra had improved erections that allowed them to have intercourse.<sup>1</sup> Initial studies show Levitra and Cialis have rates of success similar to those of Viagra.<sup>2</sup> Viagra has been studied extensively and used by millions of men; its side effects and long-term effects are well recognized. Levitra and Cialis are new drugs in which long-term effects have not been studied.

PDE-5 inhibitors should be taken at least an hour before you plan to be sexually active.

One study found that Cialis, called "the weekend pill," enhanced the ability to have erections for 24 to 36 hours after taking it.<sup>3</sup> Viagra and Levitra usually enable a man to get an erection at any time for 4 or more hours after taking it.

Viagra does not work as well as it would otherwise if you eat a high-fat meal around the time you take it, so many doctors recommend you take it on an empty stomach. Levitra may be slightly less effective if you eat a high-fat meal, but a moderate-fat meal does not reduce its effectiveness; Cialis works without regard to what you eat.<sup>4</sup>

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## Side Effects

Do not take PDE-5 inhibitors if you are taking any medication that contains nitrates, such as nitroglycerin. This combination can lower blood pressure dangerously, possibly leading to a stroke, a heart attack, or death. If you are taking a medication called an alpha-blocker—used to treat high blood pressure or an enlarged prostate—check with your health professional before you take a PDE-5 medication.

Other side effects are fairly uncommon when taking PDE-5 inhibitors. They include:

Headache.

Skin flushing.

Indigestion.

Nasal congestion.

A few men find that PDE-5 inhibitors affect their vision for a few hours after taking it, usually by causing a slight bluish tinge to their vision. A few men become more sensitive to light. These effects go away in a few hours.

See Drug Reference for a full list of side effects. (Drug Reference is not available in all systems.)

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## What To Think About

Health experts have debated the use of PDE-5 inhibitors in men with heart disease, because deaths have been reported in men who used Viagra. The 1999 American College of Cardiology/American Heart Association (ACC/AHA) Expert Consensus Document noted that PDE-5 inhibitors may be dangerous for people who:<sup>5</sup>

- Have coronary artery disease (CAD).
- Have heart failure and low blood pressure.
- Are taking many different drugs for high blood pressure.

However, several studies have reported that some men with heart problems may be able to take PDE-5 inhibitors safely.

One study found no evidence of increased risk of heart attack or CAD in men who use Viagra.<sup>6</sup> Another study in men with CAD reported that Viagra does not lead to heart attack and that heart attacks and other cardiovascular problems reported after taking Viagra may be related more to the physical activity of intercourse than to the medication.<sup>7</sup> A study of 35 men found that Viagra is safe for men with moderate heart failure.<sup>8</sup>

Sexual activity is exercise. If you have a heart condition and have not been sexually active for a while, talk with your health professional to make sure you can safely engage in sexual activity.

PDE-5 inhibitors are not prescribed for anyone who may take nitroglycerin in an emergency.

Tell your health professional if you are using PDE-5 inhibitors and are going to have a test for heart disease (such as a stress treadmill test, cardiac catheterization, stress thallium, or stress echocardiography). You should avoid taking PDE-5 inhibitors for 24 to 48 hours before such a test.

When considering PDE-5 inhibitors for erection problems, it is important to include your partner in your discussions.

If you take any medications, discuss PDE-5 inhibitors with your health professional before using them.

PDE-5 inhibitors can be prescribed by any doctor. You do not have to see a doctor who specializes in sexual health. PDE-5 inhibitors are also available on the Internet; if you obtain the medication through this route, you should discuss its use with your doctor.

Viagra costs \$8 to \$10 per pill, and not all insurance plans will cover the cost of the medication. Most insurance plans that do cover Viagra will approve only a limited supply.

Complete the new medication information form to help you understand this medication.

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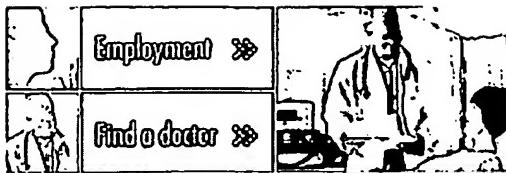
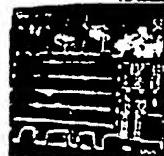
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# Type 2 Diabetes: Living With Complications



## Medications

You may be taking more than one oral medication to treat your type 2 diabetes. You may be taking insulin by injection or through an insulin pump alone or along with oral diabetes medication. Taking these medications as prescribed can help keep your blood sugar levels within your target range. For information on these medications, see the Medications section of the topic Type 2 Diabetes: Living With the Disease.

You may need to take:

- Aspirin. If you are age 30 or older, talk to your health professional about taking a low-dose, or baby, aspirin daily to prevent heart attack, stroke, or other large blood vessel disease (macrovascular disease).<sup>1</sup>
- An angiotensin-converting enzyme (ACE) inhibitor, angiotensin II receptor blocker, or other medication if you have high blood pressure or have protein in your urine. These medications can slow or prevent further damage to your kidneys.
- Medications for digestive problems. The type of medication will depend on the problem you are having. For example, if you have gastroparesis, you may take metoclopramide (Reglan), domperidone (available in Europe and Canada), or erythromycin.
- Nonprescription pain relievers, creams, or prescription oral or injection medications if you have pain from peripheral neuropathy.
- Viagra, Levitra, or Cialis if you have erection problems. These medications can aggravate heart problems in some people, especially those taking nitrate medications (such as nitroglycerin). Check with your doctor before taking any of these medications.

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## **Medication Choices**

Medications for some complications include:

- Aspirin after a heart attack or stroke or to prevent these.
- Statins such as atorvastatin (Lipitor), simvastatin (Zocor), or pravastatin (Pravachol), to help prevent heart attack or stroke.
- Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for diabetic nephropathy.
- Phosphodiesterase-5 inhibitors (PDE-5 inhibitors), such as Viagra, Levitra, or Cialis if you have erection problems. Check with your doctor before taking any of these medications.

## **What to Think About**

Keep your blood sugar levels tightly within a safe range by taking your oral diabetes medication (and, in some cases, insulin) as prescribed.

If you have high cholesterol, take cholesterol-reducing medications (such as statins) to keep your LDL cholesterol level less than 100 mg/dL (2.60 mmol/L), your triglyceride level less than 150 mg/dL (1.7 mmol/L), and if possible, your HDL cholesterol level more than 40 mg/dL (1.15 mmol/L) in men. Women may need an HDL level of more than 50 mg/dL.<sup>7</sup> See the topic High Cholesterol.

If you have high blood pressure, take medications to keep your blood pressure consistently below 130/80 mm Hg. If your systolic blood pressure is between 130 mm Hg and 139 mm Hg or your diastolic blood pressure is between 80 mm Hg and 89 mm Hg, you may try some lifestyle or behavioral therapy for 3 months before starting medication.<sup>6</sup> For more information, see the topic High Blood Pressure (Hypertension).

---

Author: Marianne Flagg Last Updated April 27, 2004

Medical Review: Caroline S. Rhoads, MD - Internal Medicine  
Alan Dalkin, MD - Endocrinology

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